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PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS OF THE M-258A--ETC(U)
SEP 81 J T FRUIN, M A HANES
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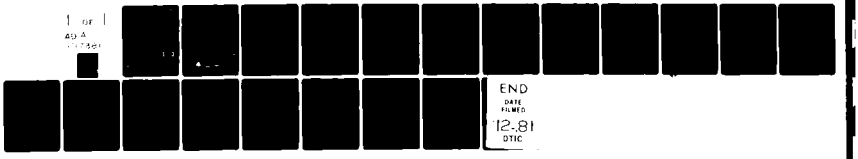

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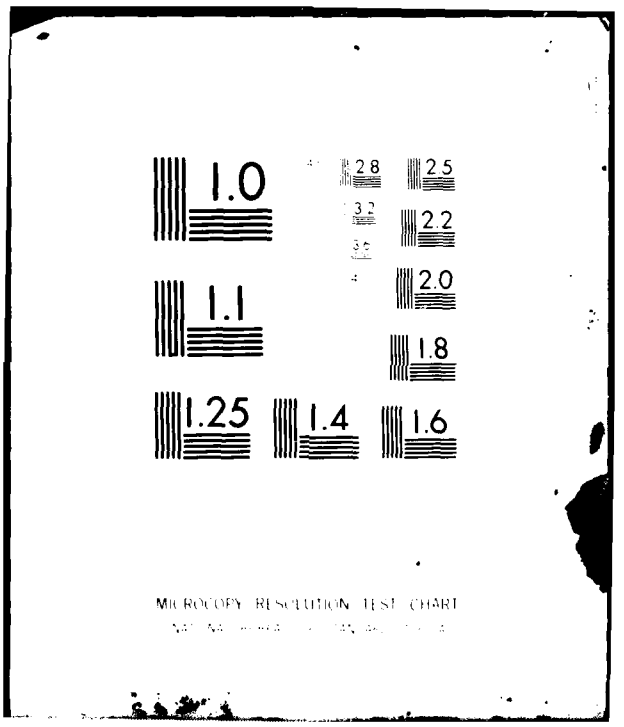
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MICROCOPY RESOLUTION TEST CHART

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M-258A-1 Kit, Primary Dermal Irritation, Chemical Defense, Chemical Decontamination

20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

The dermal irritation potential of components of the Prototype M-258A-1 Decontamination Kit was assessed by using a modified Draize test. The test called for applying the components to be wiped on the skin as they are intended to be applied under field conditions. Both components, Decon I and Decon II, when applied separately and together caused mild irritation after exposure and occlusion for 24 hr.

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PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS OF THE M-258A-1 DECONTAMINATION KIT (Study 2)

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and
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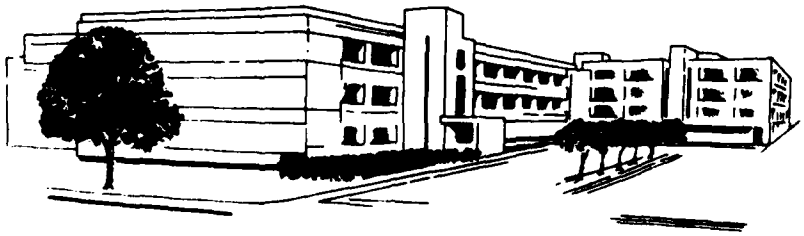
TOXICOLOGY GROUP,
DIVISION OF RESEARCH SUPPORT

SEPTEMBER 1981

Toxicology Series 8



LETTERMAN ARMY INSTITUTE OF RESEARCH PRESIDIO OF SAN FRANCISCO CALIFORNIA 94129

Toxicology Series 8

In conducting the research described in this report, the investigation adhered to the "Guide for the Care and Use of Laboratory Animals," as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care, Institute of Laboratory Animal Resources, National Research Council.

This material has been reviewed by Letterman Army Institute of Research and there is no objection to its presentation and/or publication. *The opinions or assertions contained herein are the* private views of the author(s) and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense. *(AR 360-5)*

(Signature and date)

PREFACE

Primary Dermal Irritation GLP Study Report

TESTING FACILITY: Letterman Army Institute of Research
Presidio of San Francisco, CA 94129

SPONSOR: Letterman Army Institute of Research
Presidio of San Francisco, CA 94129

PROJECT: Medical Defense Against Chemical Agents 612772.875.

GLP STUDY NUMBER: 81018

STUDY DIRECTOR: LTC (P) John T. Fruin, DVM, PhD, VC, Diplomate of American College of Veterinary Preventive Medicine

PRINCIPAL INVESTIGATOR: CPT Martha A. Hanes, DVM, VC

RAW DATA: A copy of the final report, study protocol, raw data, and standard operating procedures will be retained in the LAIR Archives.

TEST SUBSTANCES:

A. Decon I, consisting of a pad pre-wetted with hydroxyethane (ethanol) 72 $\pm$ 2% phenol 10 $\pm$ 0.5%, sodium hydroxide 5 + 0.5%, ammonium hydroxide 0.2 $\pm$ 0.05% and water was used to wipe the back of rabbits for 1 minute.

B. Decon II, consisting of a pad impregnated with a quantity of crystalline chloramine B and an equal quantity of liquid contained in breakable glass ampoules covered with nylon mesh. The liquid containes hydroxyethane (ethanol) 45 $\pm$ 2%, zinc chloride 5$\pm$0.5% and water. Just prior to dosing the ampoules were broken and thus the chloramine B impregnated pad was saturated with liquid. Decon II was used to wipe the backs of rabbits for 2-3 min.

C. Decon I and Decon II were used to wipe the same area of the back for 1 and 2-3 minutes, respectively.

D. Control (no treatment)

WORK UNIT: 302 Studies on Potential Dermal Irritation of M-258A-1 Kit

PURPOSE: The purpose of this study was to determine the primary dermal irritation potential of the test substance used as listed above.

ACKNOWLEDGMENTS

The authors wish to thank LTC Kenneth Black MD, MC; CPT Warren Jederberg, MS; SSG Lance White; SP4 Thomas Kellner, BA; PFC Evelyn Zimmerman; and Carolyn Lewis, MS; for assistance in preforming the research, and for advice in scoring the irritation reactions. The authors also wish to thank LTC (P) E. Houston PhD, MS; LTC R. Howarth, VMD, VC; M. Mershon, VMD; of the U.S. Army Biomedical Laboratory Edgewood Arsenal, Aberdeen, MD, for providing prototype M-258A-1 Decontamination Kits and background information.

Signatures of Principal Scientists Involved
In The Study

We, the undersigned, believe the study, GLP Study number 81018, described in this report to be scientifically sound and the results and interpretation to be valid. The study was conducted to comply, to the best of our ability, with the Good Laboratory Practice Regulations for Nonclinical Laboratory Studies outlined by the Food and Drug Administration.

Martha A. Hanes 21 Aug 87 / John T. Fruin 19 Aug 1987

MARTHA A. HANES, DVM / DATE
CPT, VC
Principal Investigator

JOHN T. FRUIN, DVM, PhD / DATE
LTC (P), VC
Study Director

DEPARTMENT OF THE ARMY
[illegible] ARMY INSTITUTE OF RESEARCH
PRESIDIO OF SAN FRANCISCO, CALIFORNIA 94129

REPLY TO
ATTENTION OF

SGRD-ULZ-QA

22 July 1981

MEMORANDUM FOR RECORD

SUBJECT: Report of GLP Compliance

I hereby certify that in relation to LAIR GLP study 81018 the following inspections were made:

11 June 1981
16 June 1981
18 June 1981

Routine inspections with no adverse findings are reported quarterly, thus these inspections are also included in the July 1981 report to management and the Study Director.

John C Johnson

JOHN C. JOHNSON
CPT, MS
Quality Assurance Officer

PRIMARY DERMAL IRRITATION POTENTIAL OF COMPONENTS
OF THE M-258A-1 DECONTAMINATION KIT (Study 2)

An evaluation of the Prototype M-258A-1 Decontamination Kit for primary dermal irritation potential by using the modified Draize test (1) was recently completed (2). That evaluation using the standard method to apply the test compound produced evidence of severe irritation potential. Further testing was determined to be necessary to determine the kits irritation potential under conditions of proposed field usage.

Deviation from standards

Rather than applying liquid test substance on gauze, liquid impregnated pads from the M-258A-1 Decontamination Kit were cut into approximately one inch squares. Decon I squares were used to wipe the test area on the backs of rabbits for 1 minute. Decon II squares were used similarly, except the wiping was for 2 minutes. For Decon I plus Decon II the test site was first wiped for 1 minute with Decon I and then for 2 minutes with Decon II.

Chemical analysis were not conducted except for measuring pH. The pH of Decon I was 10.7 - 10.8, Decon II was 6.5 - 6.6 and combined Decon I and II was 10.6 - 10.7. Chemical composition was considered to be that printed on the outer container for the prototype M-258A-1 Decontamination Kit (Table 1 and 2). Compound stability and purity are unknown.

TABLE 1 (3)

CHEMICAL ANALYSIS OF DECON I
(pH = 10.7 - 10.8)

Component	ETOH	H_2O	Phenol	NaOH	NH_4OH
%	72%±2%	q.s.	10±0.5%	5.0±0.5%	0.2±0.05%
Name	ethanol	water	phenol	sodium hydroxide	ammonium hydroxide
Molecular Structure	C_2H_6O	H_2O	C_6H_6O	NaOH	NH_4OH
Molecular Weight	46.07	18.016	94.12	40.01	35.036

TABLE 2 (3)

CHEMICAL ANALYSIS OF DECON II
(pH = 6.5 - 6.6)

	*LIQUID PORTION			*SOLID PORTION
Component	ETOH	H_2O	$ZnCl_2$	Chloramine B
%	45±2%	50±2.5%	5±0.5%	100%
Name	ethanol	water	zinc chloride	Chloramine B (N-Chlorobenzene-sulfamido-sodium)
Molecular Structure	C_2H_6O	H_2O	$ZnCl_2$	$C_6H_5Cl\ NNaO_2S$
Molecular Weight	46.07	18.016	136.29	213.64

*** Equal quantities of liquid and solid are mixed to form Decon II.**

Objective of Study

The objective of this study was to determine the primary dermal irritation potential of the Prototype M-258A-1 Decontamination Kit as it is expected to be used in the field.

METHODS

Historical Listing of Study Events

4 June 1981	Animals were clipped and held for study.
9 June 1981	Animals were weighed.
11 June 1981	Sites for exposure were randomized.
14 June 1981	Animals were close clipped and areas marked.
15 June 1981	Animals were weighed and dosed.
15-29 June 1981	Animals were observed daily, only significant or abnormal observations were recorded.
16 June 1981	Bandages removed, 24-hr post-exposure score.
18 June 1981	72-hr post-exposure score.
22 June 1981	7-day post-exposure score, weight taken.
29 June 1981	Animals were scored and weights taken. Animals were removed from the study.

Animal Data

Animal: New Zealand White Rabbits

Sex: Male

Source: Elkhorn Rabbitry

Pre-test Conditioning:

A. Transferred from GLP Study 81005, a primary eye irritation study. Animals were rested for 3 weeks after the last eye treatment

B. Animals were close clipped and test areas marked

Method of Randomization: Manual, Latin Square, SOP-OP-STX-34

Number of Animals on test: 6 animals - each animal had 4 test sites and received each of the three test treatments and a control with no treatment

Age of animals at start of study: young adults

Body Weight Range: 3-4 kg

Condition of animals at start of study: normal

Identification System: Ear marked as per SOP-OP-AGR-1

Environmental Conditions

Caging: Number/cage = 1; Type cage used = stainless steel, wire mesh bottom, battery type, no bedding, automatic flushing

Diet: Purina Certified Rabbit Chow 5322 approximately 110 g per day supplemented with about 45 g of fresh carrots

Water: Central line to cage battery with automatic lick dispensers

Temperature: 75 ± 5 F (24 ± 3 C)

Relative Humidity: 50 ± 10%

Photoperiod: 0530 - 2000 hr/day (14 1/2 hr of light)

Dosing Levels

A. Approximately 0.03-0.1 g Decon I

B. Approximately 0.03-0.1 g Decon II

C. Approximately 0.03-0.1 g and 0.3-0.1 g of Decon I and Decon II respectively.

D. Control: Nothing was applied.

Dosing Procedures

Method and frequency of administration were dictated by SOP-OP-STX-34. The backs of the animals were close clipped and divided into quadrants designated I,II,III and IV (SOP-OP-STX-34). Areas I and IV were intact on all animals, and areas II and III were abraded by making two perpendicular scratches in the stratum corneum of the skin about 1 1/2 inch long by using an escarifier. The four application sites were about 10 cm apart. A standard latin square table was used to randomize the test sites (SOP-OP-STX-34). The test substance impregnated pads were wiped over the test sites for 1,2 and 3 minutes (see deviation to standards). A plastic strip held on by elastic tape was placed around the animal to retard evaporation, and to insure skin contact by the test substance. The test substance was

in contact with the skin for 24 hours. At the end of the exposure period the wrapping was removed, the skin wiped if material was adherent and scored.

RESULTS

Six animals were exposed to the chemicals. Animals were scored at 24 and 72 hr, 7 and 14 days for edema/erythema (Table 3). Tabular data appear in Appendix A. Abraded areas (sites II and III) and intact areas (sites I and IV) were graded separately as well as together. The scores obtained were used for a basis for categorization. Primary irritation potential values were calculated from the 24-and 72-hr scores.

TABLE 3

EVALUATION OF SKIN REACTIONS (4)

Erythema and Eschar Formation	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate-to-severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injurious in depth)	4
Possible total erythema score	4*
Edema Formation	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well defined by definite raising)	2
Moderate edema (edges raised aproximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Possible total edema score	4*
Possible total score for primary irritation	8

* Any skin reaction more serious than severe erythema, severe edema, vesiculation, ulceration, or necrosis places the chemical in Category IV.

Compounds producing combined averages (intact and abraded scores) of 0.51-2 are considered mildly irritating (Category II), if the intact score is greater than 0.5 (Category assignment and interpretation, A.H. McCreesh, 1980, personnel communication).

Table 4 demonstrates the primary irritation indexes for the exposed areas.

TABLE 4

PRIMARY DERMAL IRRITATION INDEX FOR M-258A-1 DECONTAMINATION KITS

Chemical	Intact Score	Abraded Score	Combined Score	Category
Decon I	0.75	1.25	0.92	II
Decon II	1.83	0.67	1.25	II
Decon I+II	0.75	1.13	1.00	II
Control	0.33	0.17	0.25	I

DISCUSSION

Decon I, Decon II, and Decon I+II showed mild irritation potential. The irritation demonstrated by this test was much less severe than demonstrated in the test using 0.5 g of test substance (2).

CONCLUSIONS

The modified Draize test presented here may provide more accurate data concerning the potential hazard of the M-258A-1 Decontamination Kit to the soldier in the field.

RECOMMENDATIONS

Recommendations will be made after the current series of studies is completed.

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Summary of Primary Skin Irritation Test Data

		Page
APPENDIX A-1	Decon I	10
APPENDIX A-2	Decon II	11
APPENDIX A-3	Decon I and II	12
APPENDIX A-4	Control	13

APPENDIX A

APPENDIX A-1

Summary of Primary Skin Irritation Test Data

GLP Study No. 81013	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 15 June 81	Decon I	NA	NA	NA	A

Principal Investigator CPT HANES

Irritation Scores

		Intact Skin Sites				Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100044	I	0	0	0	0					
F8100052						II	1	2	0	0
F8100054	IV	0	1	0	0					
F8100057						III	1	1	0	0
F8100061	I	0	0	0	0					
F8100076	IV	1	2	1	1					
Total:		a 1	b 3	a 1	b 1		a 2	b 3	a 0	b 0
		a+b 4		a+b 2			a+b 5		a+b 0	
		C^I + 6					C^A + 5			

Intact Score = $C^I / 2 \times$ No. of Sites on test 6/(2x4) = .75

Abraded Score = $\frac{C^A}{2 \times \text{No. of Sites on test}}$ 5/(2x2) = 1.25

Total Score = $\frac{C^I + C^A}{2 \times \text{No. of Sites on test}}$ 11/(2x6) = 0.92

Primary Skin Irritation Index Category II

Remarks:

APPENDIX A-2

Summary of Primary Skin Irritation Test Data

GLP Study No. 81018	Chemical Name	Conc	Solvent	Art Applied	Code
Date of Application 15 July 1981	Decon II	NA	NA	NA	

Principal Investigator CPT HANES

Irritation Scores

		Intact Skin Sites				Abraded Skin Sites				
Rabbit no.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100044						II	0	0	0	0
F8100052	I	1	1	2	1					
F8100054						III	0	1	0	1
F8100057	IV	0	0	1	0					
F8100061						II	0	2	0	0
F8100076	I	1	3	0	1					
Total:		a 2	b 4	a 3	b 2		a 0	b 3	a 0	b 1
		a+b 6		a+b 5			a+b 3		a+b 1	
		C^I + 11					C^A + 4			

Intact Score = C^I / 2xNo. of Sites on test 11/(2x3) = 1.83

Abraded Score = C^A / 2xNo. of Sites on test 4/(2x3) = 0.67

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ 15/(2x6) = 1.25

Primary Skin Irritation Index Category II

Remarks:

APPENDIX A-3

Summary of Primary Skin Irritation Test Data

GLP Study No. 81018	Chemical Name	Conc	Solvent	Amt Applied	Code
Date of Application 15 June 1981	Decon I+II	NA	NA	NA	C

Principal Investigator CPT HANES

Irritation Scores

		Intact Skin Sites				Abraded Skin Sites				
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100044						III	0	0	0	0
F8100052	IV	0	1	0	0					
F8100054	I	0	0	1	1					
F8100057						II	0	2	0	0
F8100061						III	0	0	0	0
F8100076						II	1	3	1	2
Total:		a 0	b 1	a 1	b 1		a 1	b 5	a 1	b 2
		a+b 1		a+b 2			a+b 6		a+b 3	
		C^I = 3					C^A = 9			

Intact Score = C^I / 2xNo. of Sites on test 3/(2x2) = 0.75

Abraded Score = C^A / 2xNo. of Sites on test 9/(2x4) = 1.13

Total Score = $\frac{C^I+C^A}{2 \times \text{No. of Sites on test}}$ 12/(2x6) = 1.0

Primary Skin Irritation Index Category II

Remarks:

APPENDIX A-4

Summary of Primary Skin Irritation Test Data

GLP Study No. 81018	Chemical Name	Conc	Solvent	Amt. Applied	Code
Date of Application 15 June 81	Control	NA	NA	NA	D

Principal Investigator CPT HAWES

Irritation Scores

		Intact Skin Sites					Abraded Skin Sites			
Rabbit No.	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr	Site	Erythema 24 hr	Erythema 72 hr	Edema 24 hr	Edema 72 hr
F8100044	IV	0	0	0	0					
F8100052						III	1	0	0	0
F8100054						II	0	0	0	0
F8100057	I	1	1	0	0					
F8100061	IV	0	0	0	0					
F8100076						III	0	0	0	0
Total:		a 1	b 1	a 0	b 0		a 1	b 0	a 0	b 0
		a+b 2		a+b 0			a+b 1		a+b 0	
		C^I = 2					C^A = 1			

Intact Score = C^I / 2xNo. of Sites on test 2/(2x3) = 0.33

Abraded Score = C^A / 2xNo. of Sites on test 1/(2x3) = 0.17

Total Score = $\frac{C^I + C^A}{2 \times No.}$ of Sites on test 3/(2x6) = 0.25

Primary Skin Irritation Index Category I

Remarks:


DA
FIL
12